

Preliminary Amendment

Page 2 of 3

Applicant(s): Dominic E. Cosgrove

Serial No.: 09/970,318

Confirmation No.: 1885

Filed: October 3, 2001

For: IMMUNODIAGNOSTIC DETERMINATION OF USHER SYNDROME TYPE IIA

a1
Hmani et al., *Eur. J. Hum. Genet.*, 7:363-367 (1999)). These new genes have been given the designation USH2B and USH2C, leaving USH2A to refer to the original 1q41 locus.

Please replace the paragraph beginning at page 37, line 1, with the following rewritten paragraph. Per 37 C.F.R. §1.121, this paragraph is also shown in Appendix A with notations to indicate the changes made.

Identification of Tissues that Express Usherin mRNA and Protein.

a2
Usherin is a large glycoprotein with a predicted molecular weight of 170-180 kilodaltons (Eudy et al., *Science*, 280:1753-1757 (1998)). The basic structure of the molecule is illustrated in Figure 1. This figure denotes the peptides used as immunogens for the production of antibodies used in these studies, and the portions of the molecule expressed as domain-specific fusion peptides for the protein-protein interaction studies presented. The leader peptide is followed by a 300 amino acid domain with no identifiable homologies. The next 200 amino acids comprise an LN module with homology to LN domains found in the laminin family of basement membrane glycoproteins (Bruch et al., *Eur. J. Biochem*, 185:271-279 (1989), Yurchenco et al., *J. Biol. Chem.*, 268:17286-17299 (1993)), followed by a 500 amino acid stretch containing 10 LE domains, which are rod-like laminin-EGF-like modules (Bork et al., *Q. Rev. Biophys*, 29:119-167 (1996); Beck et al., *FASEB J.*, 4:148-160 (1990)), arranged in tandem. The LE domains are followed by four repeating units of about 100 amino acids each with structural homology to fibronectin type III domains. Fibronectin type III domains are shared by at least 45 different families of molecules, and are dissimilar at the amino acid level, but have very similar and identifiable tertiary structures (Sharma et al., *EMBO J.*, 18:1468-1479 (1999)).